

**ZINC FINGER PROTEIN DERIVATIVES  
AND METHODS THEREFOR**

**ABSTRACT**

Zinc finger proteins of the Cys,His, type represent a class of malleable DNA binding

5       proteins which may be selected to bind diverse sequences. Typically, zinc finger  
proteins containing three zinc finger domains, like the murine transcription factor Zif268  
and the human transcription factor Sp1, bind nine contiguous base pairs (bp). To create  
a class of proteins which would be generally applicable to target unique sites within  
complex genomes, the present invention provides a polypeptide linker that fuses two  
10      three-finger proteins. Two six-fingered proteins were created and demonstrated to bind  
18 contiguous bp of DNA in a sequence specific fashion. Expression of these proteins  
as fusions to activation or repression domains allows transcription to be specifically up  
or down modulated within cells. Polydactyl zinc finger proteins are broadly applicable  
as genome-specific transcriptional switches in gene therapy strategies and the  
15      development of novel transgenic plants and animals. Such proteins are useful for  
inhibiting, activating or enhancing gene expression from a zinc finger-nucleotide binding  
motif containing promoter or other transcriptional control element, as well as a structural  
gene or RNA sequence.

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